REMARKS

1. Disposition of Claims

Claims 20, 22, and 23 are pending in this application. The amendments to the claims are: NONE. No new matter has been added. Reexamination and reconsideration of the application, as amended, are respectfully requested.

2. Compliance with 35 USC 112/1 enablement

The Patent Office rejected the claims under 35 USC 112/1 as failing to meet the enablement requirement. Under MPEP 2164, the test for enablement is whether one skilled in the art could make or use the subject matter defined by the claims without undue experimentation. Under MPEP 2164.01(a), the Wands factors are to be considered in determining whether any necessary experimentation is undue. Here, the specification is enabling with respect to the claimed method of producing a bacteriophage able to delay inactivation by an animal's host defense system (HDS), comprising genetically engineering a bacteriophage to express molecules on its surface coat that delay inactivation of the bacteriophage by an animal's host defense system (HDS).

i) First, there is considerable direction and guidance in the specification with respect to how to make and use the subject matter defined in the claims.

It seems to be undisputed that: The invention solves the problem in the prior art of the use of bacteriophage to fight infections caused by bacteria. One explanation for bacteriophage not always working was because the viruses were inactivated by the host defense system (HDS). To solve this problem, the inventors developed a technology to produce bacteriophage that may be serially passaged or genetically modified to delay inactivation by the host defense system (HDS).

It seems to be undisputed that: Using the serial passage technology, the inventors developed long-circulating bacteriophage that are greatly superior to wild-types in terms of rescuing animals from otherwise fatal infections. These results were published as the post-filing date inventor-created art of Merril et al., Proc Natl Acad Sci USA 93: 3188 (1996), of record.

It seems to be undisputed that: Using the genetic engineering technique, the inventors proceeded to demonstrate that the mutation in the major phage capsid (E) protein, which resulted in the change of the acidic amino acid glutamate to the basic amino acid lysine at residue 158,

conferred the "long-circulating" phenotype. The inventors identified the mutation and then incorporated this mutation into a wild-type background. These results were published as the post-filing date inventor-created art of Vitiello et al., Virus Res 114: 101 (2005), of record.

It seems to be undisputed that: In short, the inventors were able to duplicate the solution to the host defense problem afforded by the serial passage technique with the genetic engineering technology.

The Patent Office maintained the rejection of the claims under 35 USC 112/1 as failing to meet the enablement requirement on the reasoning that that there is no teaching in the specification nor in subsequent non-patent literature that the claimed genetic engineering method was ever attempted or if attempted was ever successful in producing phages that are capable of evading a host defense system (HDS). The rejection is respectfully traversed. Not only is there a teaching in the specification, which is prophetic (fusion coat proteins), but also there is a corroboration in the subsequent non-patent scientific literature of Vitiello et al. demonstrating that the claimed genetic engineering method, besides being attempted (mutein coat proteins), was actually successful in producing phages that are capable of evading a host defense system (HDS).

The Patent Office cited p. 12 of the specification:

> "An altogether different method to achieve the desired result is to genetically engineer a phage so that it expresses molecules on its surface coat, where said molecules **antagonize, inactivate, or in some other manner impede** those **actions of the HDS** that would otherwise reduce the **viability of the administered phages**." [Emphases added.]

First, contrary to the position that there is no demonstration by Vitiello et al of involvement by the "innate immune system", per p. 103, col. 1, last sentence of sec. 1, Vitiello et al expressly concludes that the data show that the single amino acid substitution in the lambda capsid E protein was sufficient to evade the "innate immune system".

Second, contrary to the position that there is no literal teaching in the specification of point mutations to naturally occurring phage coat proteins, per p. 12 of the specification, first sentence, genetic engineering of a phage so that it expresses molecules on its surface coat, where said molecules antagonize, inactivate, or in some other manner impede those actions of the HDS,

includes within this class the species of point mutations in naturally occurring phage coat proteins.

Third, contrary to the position that there is no demonstration by Vitiello et al of reduced "viability" of the phage, per the title, Vitiello et al expressly concludes that the data show "survival", i.e., viability, of phage.

Thus, with respect to p. 12 of the specification, cited by the Patent Office:

> "An altogether different method to achieve the desired result is to genetically engineer a phage so that it expresses molecules on its surface coat, where said molecules **antagonize, inactivate, or in some other manner impede** those **actions of the HDS** that would otherwise reduce the **viability of the administered phages**." [Emphases added.]

Per Vitiello et al, the experiments with regard to one embodiment of the invention have actually been performed to date, mutein coat proteins. Per Example 4, as permitted by MPEP 608.01(p) allowing prophetic (or paper) examples, another manner and process of making a different embodiment of the invention, which has not actually been conducted may nevertheless be performed, fusion coat proteins. Therefore, not only is there a teaching in the specification, which is prophetic (fusion coat proteins), but also there is a corroboration in the subsequent non-patent scientific literature of Vitiello et al. demonstrating that the claimed genetic engineering method, besides being attempted (mutein coat proteins), was actually successful in producing phages that are capable of evading a host defense system (HDS).

ii) Second, there was a high level of skill in the art at the time the application was filed. The level of skill in the molecular biology art was that of a postdoctoral fellow working in the laboratory. *Amgen Inc. v. Hoechst Marion Roussel Inc.*, 57 USPQ2d 1449, 1518 (D. Mass. 2001). Thus, the level of skill in the art was high.

iii) Third, all of the methods needed to practice the invention were well known. As of the 5 April 1994 priority date, for guidance regarding such conditions, see, for example, Sambrook, et al., 1989, Molecular Cloning, A Laboratory Manual, Cold Spring Harbor Laboratory Press, New York; and Ausubel et al., 1989, Current Protocols in Molecular Biology, Green Publishing Associates, Inc., and Wiley & Sons, Inc., New York.

iv) Per MPEP 2164.01(a), the In re Wands Court held that the specification was enabling with respect to the claims at issue and found that "there was considerable direction and guidance" in the specification; there was "a high level of skill in the art at the time the application was filed;" and "all of the methods needed to practice the invention were well known." Similarly, here, as indicated above, there was considerable direction and guidance in the specification; there was a high level of skill in the art at the time the application was filed; and all of the methods needed to practice the invention were well known. Thus, here, considering all the factors related to the enablement issue, it must be concluded that it would *not* require undue experimentation to make and use the subject matter defined in the claims. The conclusion is the claims are in compliance with 35 USC 112/1 as meeting the enablement requirement.

3. Compliance with 35 USC 112/1 written description

The issue is whether the claims are in compliance with the 35 USC 112/1 written description requirement. Under MPEP 2163, original claims constitute their own description. The pending claims are all originals (having been amended and then amended back to reconstitute the original claims), except for Claim 22, which nevertheless merely added clarification that went to its form rather than the content of the claim. Thus, these claims constitute their own description.

4. Rescission and Retraction of Prior Traversal of Restriction Requirement

The claims of the present application were subject to a restriction requirement. In response to the restriction requirement, Applicant elected without traverse. To the extent that a traversal is nevertheless in any way deemed to be explicit or implied, Applicant hereby rescinds and retracts any such traversal.

5. No Disclaimers or Disavowals

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, the Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. The Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present

disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that the Applicants have made any disclaimers or disavowals of any subject matter supported by the present application.

CONCLUSION

Applicant respectfully requests that a timely Notice of Allowance be issued in this case. If any points remain that can be resolved by telephone, the Examiner is invited to contact the undersigned at the below-given telephone number.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 11/14/07

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AMEND

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